



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Pantoliano *et al.*

Appl. No. 10/057,940

Filed: January 29, 2002

For: **High Throughput Method for
Functionally Classifying Proteins
Identified Using a Genomics
Approach**

Confirmation No.: 4865

Art Unit: 1627

Examiner: To Be Assigned

Atty. Docket: 1503.0310002

Second Preliminary Amendment and Submission of Sequence Listing

Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Notice to File Corrected Application Papers mailed March 4, 2002, Applicants submit the following Amendment to the Specification and Drawings, with accompanying Remarks. Applicants also submit an Amendment to the claims.

This Amendment is provided in the following format:

(A) A clean version of each replacement paragraph/section/claim along with clear instructions for entry;

(B) Starting on a separate page, appropriate remarks and arguments. 37

C.F.R. § 1.121 and MPEP 714; and

(C) Starting on a separate page, a marked-up version entitled: "Version with markings to show changes made."

It is not believed that extensions of time or fees for net addition of claims are required beyond those that may otherwise be provided for in documents accompanying this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned

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under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

Amendments

In the Specification:

Please substitute the current version of the text starting on page 28, line 17 and ending on page 29, line 5 with the following text:

-AT-rich tracts:

- d(T)₃₂/d(A)₃₂ (SEQ ID NO: 1)
- d(ATAT)₈/d(TATA)₈ (SEQ ID NO: 2)
- d(AAAT)₈/d(TTTA)₈ (SEQ ID NO: 3)
- d(AAATT)₆/d(TTTAA)₆ (SEQ ID NO: 4)
- d(AAATTT)₆/d(TTTAAA)₆ (SEQ ID NO: 5)
- d(AAAATTTT)₄/d(TTTTAAAA)₄ (SEQ ID NO: 6)

-GC-rich tracts:

- d(C)₃₂/d(G)₃₂ (SEQ ID NO: 7)
- d(GCGC)₈/d(CGCG)₈ (SEQ ID NO: 8)
- d(GGGCCC)₆/d(CCCGGG)₆ (SEQ ID NO: 9)
- d(GGGGCCCC)₄/d(CCCCGGGG)₄ (SEQ ID NO: 10)

-other

- d(CA)₃₂/d(GT)₃₂ (SEQ ID NO: 11)
- d(CT)₃₂/d(GA)₃₂ (SEQ ID NO: 12)
- d(AG)₃₂/d(TC)₃₂ (SEQ ID NO: 13)

-Single-stranded components of the above duplex sequences.

-d(T)₄₀/d(A)₂₀ (SEQ ID NO: 14) (an example of a fragment containing both single-stranded and duplex DNA)

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In the Claims:

Please substitute the following claim 33 for the currently pending claim 33:

33. (Once Amended) A method for determining at least one previously unidentified biological function of a target protein comprising:

(a) screening a multiplicity of different molecules from a first list of molecules for their ability to modify the stability of a target protein, wherein said first list of molecules are known to modify the stability of a group of proteins which share biological function, and wherein modification of the stability of said target protein by a molecule indicates that the molecule binds to said target protein;

(b) generating, from step (a), a second list of molecules that modify the stability of said target protein;

(c) determining if any molecule in said first list from step (a) is included in said second list from step (b), thereby determining at least one previously unidentified biological function of said target protein.

Please substitute the following claim 34 for the currently pending claim 34:

34. (Once Amended) The method of claim 33, wherein said screening step (a) comprises:

(a1) contacting said target protein with one or more of said multiplicity of different molecules in each of a multiplicity of containers;

(a2) treating said target protein in each of said multiplicity of containers to cause said target protein to unfold;

(a3) measuring in each of said containers a physical change associated with the unfolding of said target protein;

(a4) generating an unfolding curve for said target protein for each of said containers; and

(a5) comparing each of said unfolding curves in step (a4) to (1) each of said other unfolding curves and to (2) the unfolding curve obtained for said target protein in the absence of any of said multiplicity of different molecules; and

(a6) determining whether any of said multiplicity of different molecules modifies the stability of said target protein, wherein a modification in stability is indicated by a change in said unfolding curve.

Please substitute the following claim 36 for the currently pending claim 36:

36. (Once Amended) A method for determining at least one previously unidentified biological function of a target protein comprising:

(a) screening a multiplicity of different molecules for their ability to shift the thermal unfolding curve of a target protein, wherein a shift in the thermal unfolding curve of said target protein by a molecule indicates that the molecule binds to said target protein;

(b) generating, from step (a), a first list of molecules that shift the thermal unfolding curve of said target protein;

(c) comparing said first list from step (b) to at least one second list of molecules, wherein said second list of molecules are known to modify the stability of a group of proteins which share biological function; and

(d) determining if any molecule in said first list from step (b) is included in said second list from step (c), thereby determining at least one previously unidentified biological function of said target protein.

Please substitute the following claim 37 for the currently pending claim 37:

37. (Once Amended) The method of claim 36, wherein said screening step (a) comprises:

(a1) contacting said protein with one or more of said multiplicity of different molecules in each of a multiplicity of containers;

(a2) heating said multiplicity of containers from step (a1);

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(a3) measuring in each of said containers a physical change associated with the thermal unfolding of said target protein resulting from said heating;

(a4) generating a thermal unfolding curve for said target protein as a function of temperature for each of said containers; and

(a5) comparing each of said unfolding curves in step (a4) to (1) each of said other thermal unfolding curves and to (2) the thermal unfolding curve obtained for said protein in the absence of any of said multiplicity of different molecules; and

(a6) determining whether any of said multiplicity of different molecules shift the thermal unfolding curve of said protein.

Please substitute the following claim 38 for the currently pending claim 38:

38. (Once Amended) The method of claim 37, wherein said comparing step (a5) comprises ranking said molecules in said multiplicity of different molecules for binding to said target protein according to the ability of each of said multiplicity of different molecules to shift the thermal unfolding curve of said target protein.

Please substitute the following claim 48 for the currently pending claim 48:

48. (Once Amended) A method for determining at least one previously unidentified biological function of a target protein comprising:

(a) screening a multiplicity of different molecules from a first list of molecules for their ability to shift the thermal unfolding curve of a target protein, wherein said first list of molecules are known to modify the stability of a group of proteins which share biological function, and wherein a shift in the thermal unfolding curve of said target protein by a molecule indicates that the molecule binds to said target protein;

(b) generating, from step (a), a second list of molecules that modify the stability of said target protein;

(c) determining if any molecule in said first list from step (a) is included in said second list from step (b), thereby determining at least one previously unidentified biological function of said target protein.

Please substitute the following claim 49 for the currently pending claim 49:

49. (Once Amended) The method of claim 48, wherein said screening step (a) comprises:
- (a1) contacting said protein with one or more of said multiplicity of different molecules in each of a multiplicity of containers;
 - (a2) heating said multiplicity of containers from step (a1);
 - (a3) measuring in each of said containers a physical change associated with the thermal unfolding of said target protein resulting from said heating;
 - (a4) generating a thermal unfolding curve for said target protein as a function of temperature for each of said containers; and
 - (a5) comparing each of said unfolding curves in step (a4) to (1) each of said other thermal unfolding curves and to (2) the thermal unfolding curve obtained for said protein in the absence of any of said multiplicity of different molecules; and
 - (a6) determining whether any of said multiplicity of different molecules shift the thermal unfolding curve of said protein.

Please substitute the following claim 50 for the currently pending claim 50:

50. (Once Amended) The method of claim 49, wherein said comparing step (a5) comprises ranking said molecules in said multiplicity of different molecules for binding to said target protein according to the ability of each of said multiplicity of different molecules to shift the thermal unfolding curve of said target protein.

In the Drawings:

Please substitute the attached Figures 1A, 1B, 2-4, 5A-5D, 6A-6D, 7A-7D, and 8-12 for the pending Figures 1A, 1B, 2- 4, 5, 6, 7, and 8-12, respectively.

Sequence Listing:

Please insert the sequence listing at the end of the application.

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Remarks

The specification has been amended to direct the entry of a sequence listing after the claims of the above identified application and to provide the SEQ ID NO's next to the specific sequence. No new matter has been added by the amendment to the specification.

In accordance with 37 C.F.R. § 1.821(f), the paper copy of the Sequence Listing and the computer readable copy of the Sequence Listing submitted herewith in the above application are the same. In accordance with 37 C.F.R. § 1.821(g), this submission includes no new matter.

Applicants respectfully request that the Sequence Listing submitted herewith be introduced into the captioned application.

Applicants also submit formal drawings (Figures 1A, 1B, 2- 4, 5A-5D, 6A-6D, 7A-7D, and 8-12) to replace pending Figures 1A, 1B, 2-4, 5, 6, 7, and 8-12, respectively. No new matter has been added.

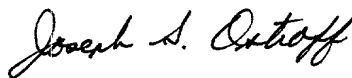
It is respectfully believed that this application is now in condition for examination. Early notice to this effect is respectfully requested.

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Further, claims 33, 34, 36-38, and 48-50 have been amended to correct minor errors. The amendment is not believed to affect the scope of the claims, and no new matter has been added. Claims 31-60 remain pending in the application. Applicants respectfully request that this Preliminary Amendment be entered.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



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Registration No. 39,321

Date: May 3, 2002

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Version with markings to show changes made

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The text starting on page 28, line 17 and ending on page 29, line 5:

-AT-rich tracts:

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-d(T)₄₀/d(A)₂₀ (SEQ ID NO: 14) (an example of a fragment containing both single-stranded and duplex DNA)

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In the Claims:

33. (Once Amended) A method for determining at least one previously unidentified biological function of a target protein comprising:

(a) screening a multiplicity of different molecules [known to bind to] from a first list of molecules for their ability to modify the stability of a target protein, wherein said first list of molecules are known to modify the stability of a group of proteins which share biological function, and wherein modification of the stability of said target protein by a molecule indicates that the molecule binds to said target protein;

(b) generating, from step (a), a second list of molecules that modify the stability of said target protein;

(c) determining if any molecule in said first list from step (a) is included in said second list from step (b), thereby determining at least one previously unidentified biological function of said target protein.

34. (Once Amended) The method of claim 33, wherein said screening step (a) comprises:

(a1) contacting said target protein with one or more of said multiplicity of different molecules in each of a multiplicity of containers;

(a2) treating said target protein in each of said multiplicity of containers to cause said target protein to unfold;

(a3) measuring in each of said containers a physical change associated with the unfolding of said target protein;

(a4) generating an unfolding curve for said target protein for each of said containers; and

(a5) comparing each of said unfolding curves in step (a4) to (1) each of said other unfolding curves and to (2) the unfolding curve obtained for said target protein in the absence of any of said multiplicity of different molecules; and

(a6) determining whether any of said multiplicity of different molecules modifies the stability of said target protein, wherein a modification in stability is indicated by a change in said unfolding curve.

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36. (Once Amended) A method for determining at least one previously unidentified biological function of a target protein comprising:

(a) screening a multiplicity of different molecules for their ability to shift the thermal unfolding curve of a target protein, wherein a shift in the thermal unfolding curve of said target protein by a molecule indicates that the molecule binds to said target protein;

(b) generating, from step (a), a first list of molecules that shift the thermal unfolding curve of said target protein;

(c) comparing said first list from step (b) to at least one second list of molecules, wherein said second list of molecules are known to modify the stability of a group of proteins which share biological function; and

(d) determining if any molecule in said first list from step (b) is included in said second list from step (c), thereby determining at least one previously unidentified biological function of said target protein.

37. (Once Amended) The method of claim 36, wherein said screening step (a) comprises:

(a1) contacting said protein with one or more of said multiplicity of different molecules in each of a multiplicity of containers;

(a2) heating said multiplicity of containers from step (a1);

(a3) measuring in each of said containers a physical change associated with the thermal unfolding of said target [molecule] protein resulting from said heating;

(a4) generating a thermal unfolding curve for said target [molecule] protein as a function of temperature for each of said containers; and

(a5) comparing each of said unfolding curves in step (a4) to (1) each of said other thermal unfolding curves and to (2) the thermal unfolding curve obtained for said protein in the absence of any of said multiplicity of different molecules; and

(a6) determining whether any of said multiplicity of different molecules shift the thermal unfolding curve of said protein.

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38. (Once Amended) The method of claim 37, wherein said comparing step (a5) comprises ranking said molecules in said multiplicity of different molecules for binding to said target protein according to the ability of each of said multiplicity of different molecules to shift the thermal unfolding curve of said target protein.

48. (Once Amended) A method for determining at least one previously unidentified biological function of a target protein comprising:

(a) screening a multiplicity of different molecules [known to bind to] from a first list of molecules for their ability to shift the thermal unfolding curve of a target protein, wherein said first list of molecules are known to modify the stability of a group of proteins which share biological function, and wherein a shift in the thermal unfolding curve of said target protein by a molecule indicates that the molecule binds to said target protein;

(b) generating, from step (a), a second list of molecules that modify the stability of said target protein;

(c) determining if any molecule in said first list from step (a) is included in said second list from step (b), thereby determining at least one previously unidentified biological function of said target protein.

49. (Once Amended) The method of claim 48, wherein said screening step (a) comprises:

(a1) contacting said protein with one or more of said multiplicity of different molecules in each of a multiplicity of containers;

(a2) heating said multiplicity of containers from step (a1);

(a3) measuring in each of said containers a physical change associated with the thermal unfolding of said target [molecule] protein resulting from said heating;

(a4) generating a thermal unfolding curve for said target [molecule] protein as a function of temperature for each of said containers; and

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(a5) comparing each of said unfolding curves in step (a4) to (1) each of said other thermal unfolding curves and to (2) the thermal unfolding curve obtained for said protein in the absence of any of said multiplicity of different molecules; and

(a6) determining whether any of said multiplicity of different molecules shift the thermal unfolding curve of said protein.

50. (Once Amended) The method of claim 49, wherein said comparing step (a5) comprises ranking said molecules in said multiplicity of different molecules for binding to said target protein according to the ability of each of said multiplicity of different molecules to shift the thermal unfolding curve of said target protein.

The Sequence Listing is added at the end of the application.

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